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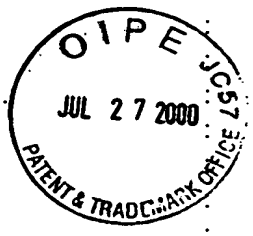

In Re Application Of	Group Art Unit 1632
LOUIS D. FALO, JR. ET AL.	Examiner Jill D. Martin
Serial No. 08/931,219	Attorney Docket No. 125350-3
Filed September 19, 1997	
Entitled	
STIMULATION OF CELL-MEDIATED IMMUNE RESPONSES BY TARGETED PARTICULATE GENETIC IMMUNIZATION	
File Wrapper Continuation of Application No. 08/535,566, filed September 28, 1995, and now abandoned.	

REPLY TO EXAMINER'S ANSWER

July 24, 2000

Assistant Commissioner for Patents
BOX AF
Washington, D.C. 20231

Sir:

This is in response to the Examiner's Answer mailed May 23, 2000 filed in the captioned case. At the outset, Appellants note with appreciation the withdrawal of the rejection of Claims 1-3, 5-17, 19-32, 34-47 and 49-61 under 35 U.S.C. § 112, second paragraph.

Grouping of Claims

The Examiner's Answer states, erroneously, that "all of the claims are argued together under each grounds of rejection." (Examiner's Answer at page 3). This is clearly not the case. On page 3 of Appellants' Brief, Appellants state general reasons as to why the claims stand or fall together. Most notably, various claims are directed to different modes of delivery that can be patentable over other modes; similarly, certain claims are directed to *in vivo* methods while others are directed to *ex vivo* methods, one of which methods could be patentable while the other not. The Argument section of the Brief does provide separate arguments for various groups of claims, in, for example, the first and second full paragraph on page 7. See also the fourth full paragraph on page 8. The Examiner even acknowledges Appellants' separate arguments regarding, for example, Claim 29. (See Examiner's Answer at page 22).

35 U.S.C. § 112, first paragraph

The Examiner's Answer indicates that Appellants' arguments are "partially persuasive" as to the rejection of Claims 1-3, 5-17, 19-32, 34-47, 49-61 and 63-71 under 35 U.S.C. § 112, first paragraph. More specifically, the Examiner's Answer indicates that the specification is enabling for methods of treating a mammalian host capable of generating an immune response, comprising producing a particulate polynucleotide comprising DNA encoding an antigen of interest on its surface and inoculating the host with the particulate polynucleotide by use of a biolistic device, direct injection or subcutaneous injection. The rejection is maintained in that the specification allegedly fails to provide enablement for "any and all routes of administration of the particulate polynucleotide or the antigen-presenting cells transfected with the particulate polynucleotide." (Examiner's Answer at page 5). While Appellants appreciate that the Examiner has finally acknowledged that the examples clearly support enablement of the biolistic approach, direct injection and subcutaneous injection, Appellants respectfully submit that the Examiner's maintenance of the rejection as it relates to other modes of administration is inconsistent and unsupported in the law.

More specifically, Appellants had previously argued, in response to the Examiner's statement that only the biolistic approach was enabled, that the examples included evidence demonstrating the efficacy of not only the biolistic approach, but also direct injection and subcutaneous injection. It does not appear, however, that this evidence was acknowledged until after submission of the Appeal Brief. Similarly, the Examiner previously maintained that only administration to the skin was enabled, but now appears to acknowledge Appellants' evidence as to the efficacy of delivery to the subcutaneum.

In any event, the Examiner's Answer cites to various references for the proposition that skin tissue is prevalent with dendritic cells, and targeting the antigen-presenting cells by routes of administration other than to the skin are not shown by either the art or the specification to be effective. The Examiner's Answer, however, then acknowledges that the specification is enabling for injection to the subcutaneum. Thus, one statement is made that administration to skin is all that is enabled, and the next statement acknowledges that injection to the subcutaneum is enabled. This position is inconsistent, and is submitted by Appellants not to be supported by the art.

The Examiner cites to the Barry reference (*Vaccine*, 1997), stating that Barry fails to support the efficacy of i.m. injection of particulate polynucleotides in delivering DNA to antigen-presenting cells. In fact, Barry does not appear to discuss inoculation with particulate polynucleotides at all, either by i.m. injection or a biolistic device; in fact, Barry appears to be inoculating with a DNA plasmid both by gene gun and i.m. injection. Appellants respectfully submit that it is therefore disingenuous to state that Barry fails to support i.m. injection of particulate polynucleotides, when Barry

does not appear to discuss injection of particulate polynucleotides by any manner; his silence cannot be extrapolated to mean a lack of support. Moreover, the Examiner cites the conclusion in Barry that the "gene gun is more effective for eliciting an immune response per unit DNA." The Examiner ignores the statements made by Barry supporting the use of i.m. injection. For example, Barry also states that "both routes of immunization can be routinely used with μg amounts of plasmid . . ." and that while the gene gun may be more efficient, "i.m. injection has its own advantages." (See Barry, page 790, column 2). In addition, the Barry article cites previous work in which it was reported that injection into various sites produced detectable immune responses; these sites included subcutaneous, intravenous, intratracheal, intrabursal, intraorbital, and intradermal. In short, the Barry article does not provide the requisite evidence that Appellants' specification lacks enablement.

Finally, the Examiner has placed an undue burden on Appellants, in requiring that their specification "provide enablement for the claimed methods encompassing **any and all** routes of administration of the particulate polynucleotide or of the antigen-presenting cells transfected with the particulate polynucleotide." (emphasis added, Examiner's Answer at page 5). Appellants submit that they have provided a disclosure sufficiently enabling such that one skilled in the art could practice the invention without undue experimentation; Appellants do not need to provide examples for "any and all" possible route of administration, or "any and all" permutations of their methods. Appellants respectfully submit that to make such a requirement is contrary to the established procedures of the Patent and Trademark Office, and fails to find support in either the case law or statutory law.

Perhaps the most significant inconsistency of all, however, is the acknowledgement by the Examiner that the present methods, when using the biolistic approach, direct injection or subcutaneous injection, are enabled by the specification, while at the same time maintaining the rejection of Claims 15-17, 19-32, 34-47, 49-61 and 63-67. *These claims specifically recite inoculation with either a biolistic device or by direct injection, which the Examiner states are enabled!* Appellants submit the rejection as to these claims is therefore clearly erroneous.

Rejections Under Section 102

Appellants maintain their position that neither Tang nor Barry teach the elicitation of a CTL response via the MHC Class I pathway, and add that such a result is not necessarily inherent in the Tang or Barry methods, as asserted in the Examiner's Answer. An external source of antigenic protein must be present in the methods of Tang and Barry to elicit an antibody response; this external source is not required according to the present methods.

The Examiner's citation to the *In re Casey* and *In re Otto* cases appears to be misplaced. Those cases are cited for the proposition "that in a claim drawn to a

process of making, the intended use must result in a manipulative difference as compared to the prior art." (Examiner's Answer at page 21). Appellants disagree with this summation; it appears that both cases stand for the proposition that methods of using a device should not be considered when determining the patentability of the device itself. In any event, the presently rejected claims are not "drawn to a process of making" nor are they related to an apparatus. Accordingly, the cases would not appear to be relevant. Nor is the citation to these cases relevant as it relates to any of the other rejections.

Appellants specifically argued that the method of Claim 29 was not taught by Tang and Barry, as the references use a gene gun whereas Claim 29 teaches direct injection. The Examiner has equated "biolistic device" and "direct injection"; as noted in a previous Response, however, this is not appropriate. The gene gun delivers particles directly to a cell, whereas direct injection using a hypodermic needle results in the deposit of particles in the extracellular fluid where APCs capable of phagocytosis absorb the particles.

Claims 1, 15, 29 and 68-71 were also rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Hui et al. Appellants had previously requested clarification from the Examiner as to whether Hui was appropriately cited under Section 102(b), as it was unclear whether the publication was more than a year prior to Appellants' filing date. The Examiner has now indicated that the relevant date of the publication is over one year before Appellants' effective filing date. Appellants note, however, that this information could have been provided by the Examiner well before the appeal stage. In any event, Hui most clearly does not teach the methods of the present invention for the reasons set forth on page 8 of the Appeal Brief.

Rejections Under 35 U.S.C. § 103

All of the claims were rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Weiner taken with either Tang or Barry. Appellants reiterate their contention that Weiner is not combinable with either Tang or Barry to render obvious the present invention, for the reasons set forth in the Appeal Brief on pages 8 and 9. In that argument, Appellants particularly noted that their methods achieve delivery of particulate polynucleotides to the APCs without the use of bupivacaine, which is apparently used by Weiner to facilitate uptake of DNA by a cell. The Examiner points out that the open ended claim language employed by Appellants does not preclude the use of such an agent. While Appellants' claims may not preclude the use of such an agent, that Appellants' methods achieve their desired elicitation of a CTL response without the use of such an agent represents an advance not taught by the art.

SUMMARY

Appellants respectfully submit that the pending claims are in condition for a Notice of Allowance based upon the arguments presented in the Appeal Brief and points of clarification made above. It is respectfully requested, therefore, that the rejection of the pending claims be reversed, and the case remanded to the Examiner for issuance of a Notice of Allowance. Such action is respectfully requested at an early date.

Respectfully submitted,

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AF/GP1632

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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

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Examiner Name	Jill D. Martin
Total Number of Pages in This Submission	
Attorney Docket Number	125350-3

ENCLOSURES *(check all that apply)*

- [ ] Fee Transmittal Form
  - [ ] Fee Attached
- [x] Amendment / Response
  - [x] After Final
  - [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
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- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Response to Missing Parts/ Incomplete Application
  - [ ] Response to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Assignment Papers *(for an Application)*
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition Routing Slip (PTO/SB/69) and Accompanying Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
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- [ ] Request for Refund
- [ ] After Allowance Communication to Group
- [ ] Appeal Communication to Board of Appeals and Interferences
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- [ ] Proprietary Information
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Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Diane R. Meyers Eckert Seamans Cherin & Mellott, LLC
Signature	
Date	July 24, 2000

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on this date: July 24, 2000

Typed or printed name	Diane R. Meyers		
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